

Remarks

Claims 1-24 and 32-47 were pending in the subject application. By this Amendment, the applicants have amended claim 32 and have canceled claims 4, 5, 8-10, 16, 17, 20-22, 35, 36, and 39-41. No new matter has been added by these amendments. Support for the amendment can be found throughout the subject application including, for example, at page 7, lines 11-13. Accordingly, claims 1-3, 6, 7, 11-15, 18, 19, 23, 24, 32-34, 37, 38, and 42-47 are now before the Examiner for consideration.

The amendments set forth herein should not be interpreted to indicate that the applicants have agreed with, or acquiesced to, the rejections as set forth in the outstanding Office Action. The claim amendments and cancellations have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. Favorable consideration of the claims now presented, in view of the remarks and amendment set forth herein, is earnestly solicited.

The subject invention advantageously provides treatment of symptoms or associated conditions of idiopathic hyperhidrosis. As defined in the application, and readily understood by the skilled artisan, idiopathic hyperhidrosis refers to a medical condition having no associated disease or cause, which is characterized by excessive, uncontrollable perspiration beyond that required to cool the body (see page 4, lines 5-10). As noted in the application, “idiopathic hyperhidrosis is often characterized as excessive sweating, usually on the palms of the hand, soles of the feet, or armpit areas, that is not caused by emotional or physical activity.” The claimed invention specifically recites using compounds that decrease the activity of serotonin receptors, such as those that affect the activity of 5-HT_{2C} receptors, to treat symptoms or associated conditions of idiopathic hyperhidrosis. The claimed invention also provides methods for prophylactically preventing or minimizing sweat secretion on a patient’s skin, especially in axillary (underarm) regions, as a result of perspiring. Such methods comprise administering therapeutic amounts of at least one compound that affects the activity of 5-HT_{2C} receptors to a patient prior to exposure to condition that is known to induce sweating (*i.e.*, hot temperature, physical activity, increased sympathetic nerve activity as a result of emotional state (*i.e.*, job interview, oral presentation)) to prevent or minimize sweating.

Despite the rejections set forth in the outstanding Office Action, no one has taught the treatment methods for idiopathic hyperhidrosis as recited in the current claims, nor have these methods even been suggested.

Claims 32-34 and 37 have been rejected under 35 U.S.C. §102(b) as being anticipated by Waldinger *et al.* (NL 1012954) (herein referred to as Waldinger I). The applicants respectfully traverse this ground for rejection because the Waldinger *et al.* I reference neither teaches nor suggests the currently claimed methods to prophylactic ally treat sweating associated with idiopathic hyperhidrosis.

For a proper rejection under 35 U.S.C. §102, a single prior art reference must, within its four corners, disclose each and every element of the claimed invention. The Waldinger I reference teaches that individuals with low levels of testosterone may suffer from hot flushes and sudation (or sweating). Specifically, Waldinger I discloses that men who have been treated for prostate cancer by orchiectomy (*i.e.*, removal of both testicles) have reduced quantity of the hormone testosterone, which “leads to a reduction in the plasma estrogen concentrations as well” (see page 3, 5th full paragraph). Hot flushes and associated perspiration have been associated with menopause, which are the result of fluctuations in estrogen levels. Waldinger I teaches that the use of 5-HT_{2A}-receptor agonists, such as mirtazapine and mianserin, on patients with low plasma concentrations of testosterone (*i.e.*, following orchiectomy) is effective in reducing hot flushes and sudation attacks (see Examples 1-5). The Waldinger I reference does not describe any method for treating patients who have normal levels of testosterone and/or estrogen hormones and have been diagnosed with idiopathic hyperhidrosis. In fact, there is no indication by the Waldinger I reference that a 5-HT_{2A} receptor activity affecting compound, such as mirtazapine, produces, or should produce, a therapeutic effect in patients where hormone levels are normal and suffer from excessive, uncontrollable perspiration that is not associated with any disease or cause (*a.k.a.*, idiopathic hyperhidrosis, as understood by the skilled artisan and defined in the subject application). Thus, it is quite clear that Waldinger I does not teach the methods as recited in the current claims.

It is basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the allegedly anticipating reference. *SSIH, supra*; *Kalman [v. Kimberly-Clarke]*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

In *Dewey v. Almy Chem. Co. v. Mimex Co.*, Judge Learned Hand wrote:

No doctrine of the patent law is better established than that a prior patent . . . to be an anticipation must bear within its four corners adequate directions for the practice [of the subsequent invention] . . . if the earlier disclosure offers no more than a starting point . . . if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge, and it is not an anticipation. 124 F.2d 986, 990; 52 USPQ 138 (2nd Cir. 1942).

As noted above, the Waldinger I reference does not disclose a beneficial method for effectively treating idiopathic hyperhidrosis, or prophylactically treating sweating associated with idiopathic hyperhidrosis, using a 5-HT_{2C} receptor activity affecting compound such as mirtazapine. Advantageously and unexpectedly, the subject application provides a unique therapeutic method for treating patients diagnosed with idiopathic hyperhidrosis where that is not associated with any disease or cause for excessive sweating. Thus, under the applicable statutory and case law, the Waldinger I reference does not anticipate the current applicants' claims. Therefore, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on the Waldinger I reference.

Claims 32-34 and 37 have been rejected under 35 U.S.C. §102(b) as being anticipated by Waldinger *et al.* (Maturitas, 2000, vol. 36, pages 165-168, herein referred to as Waldinger II). The applicants respectfully traverse this ground for rejection because the Waldinger II reference neither

teaches nor suggests the currently claimed methods to prophylactically treat sweating associated with idiopathic hyperhidrosis.

As with Waldinger I, Waldinger II teaches the use of the 5-HT_{2C} antagonist mirtazapine in treating patients with reduced plasma concentrations of the hormone estrogen. Specifically, Waldinger II demonstrates that mirtazapine is effective in treating hot flushes and night sweats in menopausal women. As readily understood by the skilled clinician and taught by Waldinger II, menopause is due to hormonal changes, namely a decline in estrogen production, and occurs normally mid- or late in one's life (see pp. 165 and 167). It also encompasses a myriad of symptoms, including hot flushes and night sweats. Waldinger II neither teaches nor suggests the use of mirtazapine in the treatment of idiopathic hyperhidrosis, nor does it teach or suggest prophylactically treating sweating associated with idiopathic hyperhidrosis, as currently claimed.

The subject invention relates to the treatment of idiopathic hyperhidrosis, including the prophylactic treatment of sweating associated with idiopathic hyperhidrosis. Idiopathic hyperhidrosis, as noted above, has no known cause. It is a life-long illness in patients with normal levels of hormones. Unlike hot flushes in menopause, which can lead to sweating/perspiration often in bouts, the sweating/perspiration experienced by patients diagnosed with idiopathic hyperhidrosis is a relatively continuous problem. In fact, as any skilled clinician understands, there is a particular sweating pattern usually associated with idiopathic hyperhidrosis (*i.e.* palms of hands, feet, as described in the instant application at p. 4, lines 9-10) and this is different from menopause related symptoms of hot flushes and night sweats, which are often localized to face, neck, and underarm regions. As such, having read both Waldinger I and II, which merely teaches the effectiveness of 5-HT_{2C} antagonists in treating hot flushes in patients with decreased levels of estrogen, the skilled artisan would not have known or even thought to use such compounds in treating patients diagnosed with idiopathic hyperhidrosis with normal estrogen and testosterone hormone levels.

As noted above, for a proper rejection under 35 U.S.C. §102, a single prior art reference must, within its four corners, disclose each and every element of the claimed invention. Because Waldinger II reference does not teach or even suggest the use of 5-HT_{2C} receptor activity affecting compounds in prophylactically treating sweating associated with idiopathic hyperhidrosis, Waldinger

II cannot anticipate the current applicants' claims. Therefore, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) of the Waldinger II reference.

Next, the applicants respectfully traverses the §103 rejections of claims set forth at pages 3-7 of the office action. The deficiencies of the Waldinger I and II references have been noted above, and are reasserted here. With regard to claims 1-3, 6, 7, 13-15, 18, 19, 32-34, 37, 38 and 44-47, Andrews *et al.* (WO 01/52855) is cited as a secondary reference to Waldinger I and II. The applicants respectfully submit that there is no *prima facie* case for obviousness. The Office Action makes a bald assertion that the skilled artisan "would have reasonably expected that mirtazapine would be symptomatically useful for treating perspiration caused by any etiologies as it has been shown that mirtazapine is particularly effective in alleviating perspiring" (see p. 4 of the Office Action). The applicants respectfully disagree. The clinician skilled in the medical arts would not have expected mirtazapine to be useful in treating perspiration by any etiologies; in fact, based on Waldinger I and II, the skilled artisan would have only expected mirtazapine to be useful only in treating hot flushes (and associated symptoms such as night sweats) in patients with decreased testosterone/estrogen levels. As noted above, unlike sweating associated with hot flushes, the sweating/perspiration experienced by patients diagnosed with idiopathic hyperhidrosis is a relatively continuous problem. In fact, as any skilled clinician understands, there is a particular sweating pattern usually associated with idiopathic hyperhidrosis (*i.e.* palms of hands, feet, as described in the instant application at p. 4, lines 9-10) and this is different from menopause related symptoms of hot flushes and night sweats, which are often localized to face, neck, and underarm regions. The Office Action provides no indication as to why the skilled artisan would have been motivated to select the Waldinger I and II references, much less modify their teachings, to arrive at the subject invention. Under these circumstances, the subject invention cannot be fairly stated to be obvious.

Further, the Andrews *et al.* does not describe any method for administering a 5-HT_{2C} activity affecting compound to patients diagnosed with idiopathic hyperhidrosis. There is no indication in the Andrews *et al.* reference that a 5-HT_{2C} activity affecting compound produces, or should produce, a therapeutic effect in patients where testosterone/estrogen hormone levels are normal and have been

diagnosed with idiopathic hyperhidrosis. Thus, the deficiencies of Waldinger I and II are not cured by Andrews *et al.*, assuming *arguendo* that a prima facie case of obviousness is established.

Regarding the rejections of claims 1-3, 6-7, 13-15, 18-19, 32-34, 37-38, and 44-47, the secondary references are Davidson *et al.* (IDS) and Andrews *et al.* over Waldinger I and II. The deficiencies of the Waldinger I and II references as well as the Andres *et al.* reference have been noted above in detail and are not cured by the Davidson *et al.* reference. The Davidson *et al.* reference merely teaches the use of fluoxetine, an antidepressant and serotonin antagonist, in treating patients with social anxiety disorders. As with Andrews *et al.*, the Davidson *et al.* reference fails to teach methods for treating idiopathic hyperhidrosis. In fact, there is no teaching or suggestion by Davidson *et al.* regarding the therapeutic efficacy of a 5-HT_{2C} activity affecting compound in treating idiopathic hyperhidrosis in patients where testosterone/estrogen hormone levels are normal and have been diagnosed with idiopathic hyperhidrosis. Thus, the deficiencies of the Waldinger I and II and Andrews references are not cured.

With regard to claims 11, 12, 23, 24, 42, and 43, the secondary references are Saadia *et al.* (IDS) and Andrews *et al.* over Waldinger I and II. The shortcomings of the Waldinger I and II and Andrews *et al.* references are not cured by Saadia *et al.* The Saadia *et al.* reference merely describes the use of intradermal botulinum injection in treating sweating (or hyperhidrosis). As with Andrews *et al.* reference, the Saadia *et al.* reference fails to teach the use of a 5-HT_{2C} activity affecting compound, such as mirtazapine, in treating idiopathic hyperhidrosis. Thus, the deficiencies of the Waldinger I and II and Andrews *et al.* references are not cured by Saadia *et al.*

Claims 11, 12, 23, 24, 42, and 43 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Waldinger I and II in view of Davidson *et al.*, Andrews *et al.*, and Saadia *et al.* As described in detail above, neither the Davidson nor the Andrews *et al.* and Saadia *et al.* references describe the use of 5-HT_{2C} activity affecting compounds, such as mirtazapine, in treating idiopathic hyperhidrosis or in prophylactically treating sweating associated with idiopathic hyperhidrosis. Because the deficiencies of the Waldinger I and II references are not cured by either Davidson *et al.*, Andrews *et al.*, or Saadia *et al.*, whether alone or in combination, a finding of obviousness is not proper.

A finding of obviousness is proper only when the prior art contains a suggestion or teaching of the claimed invention. Here, it is only the applicant's disclosure that teaches the use of 5-HT2C activity affecting compounds in treating idiopathic hyperhidrosis and in treating sweating associated with idiopathic hyperhidrosis, and the applicant's disclosure cannot be used to reconstruct the prior art for a rejection under 35 U.S.C. §103. This was specifically recognized by the CCPA in *In re Sponnoble*, 160 USPQ 237, 243 (1969):

The Court must be ever alert not to read obviousness into an invention on the basis of the applicant's own statements; that is we must review the prior art without reading into that art appellant's teachings. *In re Murray*, 112 USPQ 364 (1959); *In re Sprock*, 133 USPQ 360 (1962). The issue, then, is whether the teachings of the prior art would, in and of themselves and without the benefits of appellant's disclosure, make the invention as a whole, obvious. *In re Leonor*, 158 USPQ 20 (1968). (Emphasis in original)

The mere fact that the purported prior art could have been modified or applied in a manner to yield applicant's invention would not have made the modification or application obvious unless the prior art suggested the desirability of the modification. *In re Gordon*, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Moreover, as expressed by the CAFC, to support a §103 rejection, "[b]oth the suggestion and the expectation of success must be founded in the prior art" *In re Dow Chemical Co.*, 5 USPQ 2d 1529, 1531 (Fed. Cir. 1988). In the Waldinger I and II and secondary references, one finds neither. Because the deficiencies of the Waldinger I and II reference have not been cured by any of the secondary references relied on in the office action, the obviousness rejections set forth at pages 3-7 should be withdrawn.

The applicants respectfully submit that any suggestion to treat idiopathic hyperhidrosis using 5-HT2C activity affecting compounds could only be arrived at through hindsight reconstruction, which is improper. Accordingly, reconsideration of the obviousness rejections set forth at pages 3-7 is respectfully requested.

The applicant also invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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